

GenCore version 4.5
Copyright (c) 1993 - 2000 Compugen Ltd.

OM protein - protein search, using sw model

Run on: September 27, 2001, 16:43:31 ; Search time 16.74 seconds

(without alignments)
667.102 Million cell updates/sec

Title: US-09-483-543a-9

Perfect score: 1733
Sequence: 1 KRGCAGNDFSEBSSWYGR.....SGCGXGLEVLFGQVPRKGGXG 326

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 93435 seqs, 34255486 residues

Total number of hits satisfying chosen parameters: 93435

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Database : SwissProt_39:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	1612	93.0	304	1 CRK_MOUSE	064010 mus musculu
2	1605	92.6	304	1 CRK_RAT	063768 rattus norv
3	1588	91.6	304	1 CRK_HUMAN	P46108 homo sapien
4	1379.5	79.6	305	1 CRK_CHICK	004929 gallus gall
5	1315	75.9	296	1 CRK_XENLA	P87378 xenopus lae
6	917.5	52.9	303	1 CRKL_HUMAN	P46109 homo sapien
7	911.5	52.6	303	1 CRKL_MOUSE	P47941 mus musculu
8	818.5	47.2	440	1 GAGC_AYISC	P05433 avian sarco
9	642.5	37.1	271	1 CRK_DROME	09xyu0 drosophila
10	257	14.8	217	1 GRAP_HUMAN	013588 homo sapien
11	236	13.6	211	1 DRK_DROME	008012 drosophila
12	224	12.9	217	1 GRB2_MOUSE	060631 mus musculu
13	224	12.9	217	1 GRB2_HUMAN	007883 gallus gall
14	218	12.6	217	1 GRB2_CHICK	007883 gallus gall
15	214	12.3	217	1 GRB2_XENLA	P87379 xenopus lae
16	202	11.7	228	1 SEM5_CAEL	P29355 caenorhabdi
17	184	10.6	1291	1 PIG1_BOVIN	P08487 bos taurus
18	178	10.3	1290	1 PIG1_HUMAN	P19174 homo sapien
19	177	10.2	1290	1 PIG1_RAT	P10666 rattus norv
20	174.5	10.1	322	1 GRP2_MOUSE	089100 m gtb2-rela
21	174	10.0	845	1 VAV_HUMAN	P15498 homo sapien
22	173	10.0	845	1 VAV_RAT	P54100 rattus norv
23	167	9.6	845	1 VAV_MOUSE	P27870 mus musculu
24	159.5	9.2	330	1 VAV3_HUMAN	09ukw4 homo sapien
25	158.5	9.1	330	1 GRP2_HUMAN	075791 h gtb2-rela
26	157	9.1	520	1 ITSN_HUMAN	Q15811 homo sapien
27	155.5	9.0	847	1 VAV3_MOUSE	091068 mus musculu
28	154.5	8.9	878	1 VAV_HUMAN	P52735 homo sapien
29	151	8.7	1168	1 MYSC_ACACA	P10569 acanthamoeb
30	150	8.7	960	1 DLG1_DROME	P31007 drosophila
31	148.5	8.6	868	1 VAV2_MOUSE	060992 mus musculu
32	148.5	8.6	1113	1 MYSD_DICDI	P34109 dictyostell
33	147	8.5	1044	1 GTPA_BOVIN	P09851 bos taurus

34	146.5	8.5	1038	1 GTPA_RAT	P50904 rattus norv
35	146	8.4	946	1 RHG4_HUMAN	P98171 homo sapien
36	144.5	8.3	1047	1 GTPA_HUMAN	P20936 homo sapien
37	142	8.2	450	1 CSK_CHICK	P41239 gallus gall
38	139	8.0	359	1 YKA7_CAEL	P34258 caenorhabdi
39	139	8.0	1196	1 ABIL1_CAEL	P03949 caenorhabdi
40	138.5	8.0	505	1 SRR1_SPOLA	P42686 spongilla l
41	138.5	8.0	1265	1 PIG2_RAT	P24135 rattus norv
42	138	8.0	583	1 SHC_HUMAN	P29353 homo sapien
43	137.5	7.9	578	1 SHC_MOUSE	P98083 mus musculu
44	136	7.8	450	1 CSK_HUMAN	P41240 homo sapien
45	134	7.7	450	1 CSK_MOUSE	P41241 mus musculu

ALIGNMENTS

```

RESULT 1
ID CRK_MOUSE STANDARD; PRT; 304 AA.
AC 064010;
DT 01-NOV-1997 (rel. 35, Created)
DT 01-NOV-1997 (rel. 35, Last sequence update)
DT 15-JUL-1999 (rel. 38, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
GN CRK OR CRKO.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RX MEDLINE=94239744; PubMed=8183562;
RA Ogawa S., Toyoshima H., Kozutsumi H., Hagiwara K., Sakai R.,
RA Tanaka T., Hirano N., Mano H., Yazaki Y., Hirai H.;
RT "The C-terminal SH3 domain of the mouse c-Crk protein negatively
RT regulates tyrosine-phosphorylation of Crk associated p130 in rat 3Y1
RT cells."
RL Oncogene 9:1669-1678(1994).
RN [2]
RP X-RAY CRYSTALLOGRAPHY (1.5 ANGSTROMS) OF 134-190.
RX MEDLINE=95253821; PubMed=7735837;
RA Wu X., Knudsen B., Feller S.M., Zheng J., Sali A., Cowburn D.,
RA Hanafusa H., Kuriyan J.;
RT "Structural basis for the specific interaction of lysine-containing
RT proline-rich peptides with the N-terminal SH3 domain of c-Crk."
RL Structure 3:215-226(1995).
RN [3]
RP X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 133-191.
RX MEDLINE=99069628; PubMed=9851931;
RA Nguyen J.T., Turk C.W., Cohen F.E., Zuckermann R.N., Lim W.A.;
RT "Exploiting the basis of proline recognition by SH3 and WW domains:
RT design of N-substituted inhibitors."
RL Science 282:2088-2092(1998).
CC -!- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
CC THAT BIND TO GRB2.
CC -!- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);
CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
CC LAST 100 RESIDUES.
CC -!- TISSUE SPECIFICITY: UBIQUITOUS.
CC -!- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION (BY
CC SIMILARITY).
CC -!- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -!- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -!- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
CC the European Bioinformatics Institute. There are no restrictions on its

```

CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).

DR EMBL: S72408; AAB30755.1; -.
 DR PDB: 1CKA; 08-MAY-95.
 DR PDB: 1CKB; 08-MAY-95.
 DR PDB: 1B07; 06-JAN-99.
 DR MGD: MGI:86508; C-to.
 DR InterPro: IPR000980; -.
 DR InterPro: IPR001452; -.
 DR Pfam: PF00017; SH2; 1.
 DR Pfam: PF00018; SH3; 1.
 DR PRINTS: PRO0401; SH2DOMAIN.
 DR PRINTS: PRO0452; SH3DOMAIN.
 DR PROSITE: PS50001; SH2; 1.
 DR PROSITE: PS50002; SH3; 1.
 DR Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;
 KM Phosphorylation; 3D-structure.
 FT DOMAIN 13 118 SH2.
 FT DOMAIN 132 192 SH3.
 FT DOMAIN 256 296 SH3.
 FT VARSPIC 205 304 MISSING (IN ISOFORM CRK-1).
 SQ SEQUENCE 304 AA; 33814 MW; 5491896FC7A89065 CRC64;

Query Match 93.0%; Score 1612; DB 1; Length 304;
 Best Local Similarity 100.0%; Pred. No. 4.9e-109; Matches 303; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 5 AGNFDSEERSWYGRSLRQEAVALLOGRHGYFLVRDSTSPGDYVLSVSENSRVSHYI 64
 DB 2 AGNFDSEERSWYGRSLRQEAVALLOGRHGYFLVRDSTSPGDYVLSVSENSRVSHYI 61
 QY 65 INSSGPRPPVPPSPAPPGVSPSRIRIGDQEDSLPALLEFYKIHVLDITTLIEPVARS 124
 DB 62 INSSGPRPPVPPSPAPPGVSPSRIRIGDQEDSLPALLEFYKIHVLDITTLIEPVARS 121
 QY 125 RQSGSVILRQEAAYRALDFNGNDEEDLPFKKGDLIRIRDKPEQWMAEDSEGRGM 184
 DB 122 RQSGSVILRQEAAYRALDFNGNDEEDLPFKKGDLIRIRDKPEQWMAEDSEGRGM 181
 QY 185 IPVPEYKRRPASASVSALIGNQEGSHPOPLGPEPGRPYAQPVSNTPLPLQNGPIYAR 244
 DB 182 IPVPEYKRRPASASVSALIGNQEGSHPOPLGPEPGRPYAQPVSNTPLPLQNGPIYAR 241
 QY 245 VIKRRVPAAYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTHVRLDDQNPDE 304
 DB 242 VIKRRVPAAYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTHVRLDDQNPDE 301
 QY 305 DFS 307
 DB 302 DFS 304

RESULT 2
 CRK_RAT ID CRK_RAT STANDARD: PRT: 304 AA.
 AC 063768;
 DT 01-NOV-1997 (rel. 35, Created)
 DT 01-NOV-1997 (rel. 35, Last sequence update)
 DT 01-OCT-2000 (rel. 40, Last annotation update)
 DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
 GN CRK.
 OS Rattus norvegicus (Rat).
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
 OX NCBI_TaxID=10116;
 RN [1]
 RP SEQUENCE FROM N.A.
 RC TISSUE=Kidney;
 RX MEDLINE=97057214; PubMed=8901553;

RA Kizaka-Kondoh S., Matsuda M., Okayama H.;
 RT "CrkII signals from epidermal growth factor receptor to Ras."
 RL Proc. Natl. Acad. Sci. U.S.A. 93:12177-12182(1996).
 CC -I- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
 CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
 CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
 CC THAT BIND TO GRB2.
 CC -I- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);
 CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
 CC LAST 100 RESIDUES.
 CC -I- TISSUE SPECIFICITY: CRK-II IS EXPRESSED IN ALL TISSUES AND CELLS
 CC WHEREAS CRK-I IS EXPRESSED AT LOWER LEVEL AND IN LIMITED CELL-
 CC TYPES.
 CC -I- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
 CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
 CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION (BY
 CC SIMILARITY).
 CC -I- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -I- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -----

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).

DR EMBL: D44481; BAA07924.1; -.
 DR HSSP: Q64010; 1CKB.
 DR InterPro: IPR000980; -.
 DR InterPro: IPR001452; -.
 DR Pfam: PF00017; SH2; 1.
 DR Pfam: PF00018; SH3; 1.
 DR PRINTS: PRO0401; SH2DOMAIN.
 DR PRINTS: PRO0452; SH3DOMAIN.
 DR PROSITE: PS50001; SH2; 1.
 DR PROSITE: PS50002; SH3; 1.
 DR Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;
 KM Phosphorylation.
 FT DOMAIN 13 118 SH2.
 FT DOMAIN 132 192 SH3.
 FT DOMAIN 256 296 SH3.
 FT VARSPIC 205 304 MISSING (IN ISOFORM CRK-1).
 FT VARIANT 244 244 O -> R (NKR-23 INACTIVE MUTANT).
 FT VARIANT 253 253 K -> E (NKR-23 INACTIVE MUTANT).
 SQ SEQUENCE 304 AA; 33844 MW; 4CFBFB65BE72E265 CRC64;

Query Match 92.6%; Score 1605; DB 1; Length 304;
 Best Local Similarity 99.3%; Pred. No. 1.6e-108; Matches 301; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

QY 5 AGNFDSEERSWYGRSLRQEAVALLOGRHGYFLVRDSTSPGDYVLSVSENSRVSHYI 64
 DB 2 AGNFDSEERSWYGRSLRQEAVALLOGRHGYFLVRDSTSPGDYVLSVSENSRVSHYI 61
 QY 65 INSSGPRPPVPPSPAPPGVSPSRIRIGDQEDSLPALLEFYKIHVLDITTLIEPVARS 124
 DB 62 INSSGPRPPVPPSPAPPGVSPSRIRIGDQEDSLPALLEFYKIHVLDITTLIEPVARS 121
 QY 125 RQSGSVILRQEAAYRALDFNGNDEEDLPFKKGDLIRIRDKPEQWMAEDSEGRGM 184
 DB 122 RQSGSVILRQEAAYRALDFNGNDEEDLPFKKGDLIRIRDKPEQWMAEDSEGRGM 181
 QY 185 IPVPEYKRRPASASVSALIGNQEGSHPOPLGPEPGRPYAQPVSNTPLPLQNGPIYAR 244
 DB 182 IPVPEYKRRPASASVSALIGNQEGSHPOPLGPEPGRPYAQPVSNTPLPLQNGPIYAR 241
 QY 245 VIKRRVPAAYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTHVRLDDQNPDE 304
 DB 242 VIKRRVPAAYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTHVRLDDQNPDE 301

QY 305 DFS 307
111
Db 302 DFS 304

RESULT 3
ID CRK_HUMAN STANDARD; PRT; 304 AA.

AC P46108;
DT 01-NOV-1995 (Rel. 32, Created)
DT 01-NOV-1995 (Rel. 32, Last sequence update)
DE 01-OCT-2000 (Rel. 40, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
GN CRK.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Embryonic lung, and Placenta;
RX MEDLINE=92334347; PubMed=1630456;
RA Matsuda M., Tanaka S., Nagata S., Kojima A., Kurata T., Shibuya M.;
RT "Two species of human CRK cDNA encode proteins with distinct
RT biological activities.";
RL Mol. Cell. Biol. 12:3482-3489(1992).
RN [2]
RP SEQUENCE FROM N.A.
RX MEDLINE=93309662; PubMed=8378094;
RA Floretos T., Heisterkamp N., Groffen J., Benjes S., Morris C.;
RT "CRK proto-oncogene maps to human chromosome band 17p13.";
RL Oncogene 8:2853-2855(1993).
CC -1- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
CC THAT BIND TO GRB2.
CC -1- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);
CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
CC LAST 100 RESIDUES.
CC -1- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION
CC -1- PPM: PHOSPHORYLATION OF CRK-II (40 KDA) GIVES RISE TO A 42 KDA
CC FORM.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).

CC EMBL; D10656; BAA01505.1; -;
DR EMBL; S65701; AAB28213.1; -;
DR HSSP; Q64010; ICRB.
DR SWISS-2DPAGE; P46108; HUMAN.
DR MIM; 164762; -;
DR InterPro; IPR000980; -;
DR InterPro; IPR001452; -;
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 1.
DR PRINTS; PRO0401; SH2DOMAIN.
DR PRINTS; PRO0452; SH3DOMAIN.
DR PROSITE; PSS0001; SH2; 1.
DR PROSITE; PSS0002; SH3; 1.
KW Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;
FT DOMAIN 13 118 SH2.
FT DOMAIN 132 192 SH3.
FT DOMAIN 256 296 SH3.

FT VARSPIC 205 304 MISSING (IN ISOFORM CRK-1).
SQ SEQUENCE 304 AA; 33872 MW; D7A483ED1FC0EBC CRC64;
Query Match 91.6%; Score 1588; DB 1; Length 304;
Best local Similarity 98.7%; Pred. No. 2.6e-107;
Matches 299; Conservative 1; Mismatches 3; Indels 0; Gaps 0;

QY 5 AGNFDEERSWYGRSLRSQEAVALLOQGRHGFVLRDSTSPGQVYLSVNSRVSHTY 64
|||||
Db 2 AGNFDEERSWYGRSLRSQEAVALLOQGRHGFVLRDSTSPGQVYLSVNSRVSHTY 61
|||||
QY 65 INSSGPPPPVPSPAOPPPGVSPSRRLIDQDFDSLPALLEFYKHYLDFTTLLEPARS 124
|||||
Db 62 INSSGPPPPVPSPAOPPPGVSPSRRLIDQDFDSLPALLEFYKHYLDFTTLLEPARS 121
|||||
QY 125 ROSSGYLROEEAEYRALDFENGNDDEDLPEFKGDLIRKPEQWMAADSDSGKRG 184
|||||
Db 122 ROSSGYLROEEAEYRALDFENGNDDEDLPEFKGDLIRKPEQWMAADSDSGKRG 181
|||||
QY 185 IVPVYEKYRPASASYSALIGNQEGSHPOPLGPPGYPAPSVNTPPLNONGPIYAR 244
|||||
Db 182 IVPVYEKYRPASASYSALIGNQEGSHPOPLGPPGYPAPSVNTPPLNONGPIYAR 241
|||||
QY 245 VIGKVPNAVYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTVRLDQNPDE 304
|||||
Db 242 VIGKVPNAVYKTALALEVGLVYKTKINVSQWEGECNGKRGHPFTVRLDQNPDE 301
|||||

QY 305 DFS 307
111
Db 302 DFS 304

RESULT 4
ID CRK_CHICK STANDARD; PRT; 305 AA.

AC Q04929;
DT 01-NOV-1995 (Rel. 32, Created)
DT 01-NOV-1995 (Rel. 32, Last sequence update)
DT 01-NOV-1995 (Rel. 32, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38).
GN CRK.
OS Gallus gallus (Chicken).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC Gallus.
OX NCBI_TaxID=9031;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=93041379; PubMed=1329926;
RA Reichman C.T., Mayer B.J., Khawer S., Hanafusa H.;
RT "The product of the cellular crk gene consists primarily of SH2 and
RT SH3 regions.";
RL Cell Growth Differ. 3:451-460(1992).
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@isb-sib.ch).

CC EMBL; I08168; AAA49001.1; -;
DR HSSP; Q64010; ICRB.
DR InterPro; IPR000980; -;
DR InterPro; IPR001452; -;
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 1.
DR PRINTS; PRO0401; SH2DOMAIN.
DR PRINTS; PRO0452; SH3DOMAIN.


```
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL; X59656; CAA4219.1; -.
DR HSSP; Q64010; ICKB.
DR MIM; 602007; -.
DR InterPro; IPRO00980; -.
DR InterPro; IPRO01452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 1.
DR PRINTS; PR00401; SH2DOMAIN.
DR PRINTS; PR00452; SH3DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 1.
DR SH2 domain; SH3 domain.
KW DOMAIN 14 102 SH2.
FT DOMAIN 123 183 SH3.
FT DOMAIN 235 296 SH3.
SQ SEQUENCE 303 AA; 33777 MW; 294CF1EE2CD44B81 CRC64;
```

Query Match	52.9%;	Score	917.5;	DB	1;	Length	303;
Best Local	56.6%;	Pred. No.	3.7e-59;				
Matches	185;	Conservative	33;	Mismatches	56;	Indels	53;
						Gaps	6;

Qy 5 AGNFDSEERSMYYWGR.LSRQEAENALLQDGRHGCVFLVRPSTSGDGYLVLSVSENSRVSHI 64
3 SARFDSDRSAYMGPVSRQEAOTRLQGRHGMFLVRPSTSGDGYLVLSVSENSRVSHI 62
bb

QY 65 INSSGRPRPVPPSPAQP PPGVSPSRLLIGDGEFDSLPALEFFYKIH YLDTTTLIEPVAR- 123
||| | : ||||| ||||||| ||||||| |
Db 63 INSIPNR-----RFGIDGDEDLPALEFFYKIH YLDTTTLIEAPRY 105

QY 124 -----SRQSGVILRQEAEFYRALEDENGDEEDLPFKGDILRIKDPPEEQWNAED 177
| : :: |||| |::|| | |||||||::| | :|||||||::| :
106 HCNHCVGCAADNR DAAENR NUNHR VBNBANA NRJ DEVCVGTNDR RND 187

```

QY      178 SEGKRGMPVPVYEKYRPAASASVALICGNQEGSH----PQPLGPEPG-PIAOPSVN- 230
      :|:|||||||      |:|      |||      |||

```

231 -----"PLPNLNGPIYARIÖKRVPNAYDKITALALEVGELVYTKINVSÖM 278

Db 216 LPVSSSPGALTPLPSTONGPVEAKAIQKRVPCAYDKTALALEVGDIYKVTNRINGQW 275

QY 279 EGECSNGRGHFFTHVRLDDQNPDED 305

Db 276 EGEVNGRKGLFFPTHVKIPDPNDEN 302

RESULT	7
CRKL_MOUSE	
ID	CRKL_MOUSE
STANDARD;	
PRT;	303 AA.

DT	01-FEB-1996 (Rel. 33, Created)
DT	01-FEB-1996 (Rel. 33, Last sequence update)
DT	01-NOV-1997 (Rel. 35, Last sequence update)

DE CRK-LIKE PROTEIN.
GN CRKL OR CRKL.
OS Mus musculus (Mouse).

CC Eukaryota; Metazoa; Chordata; Chordata; Vertebrata; Euteleostomi;
 CC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.
 OX NCBI_TaxID=10090;
 PN [1]

RP SEQUENCE FROM N.A.
RC STRAIN=C57BL X CBA; TISSUE=Placenta;
RX MEDLINE=96030874; PubMed=7478571;

RT Tyrosine phosphorylation of murine Cdk1¹⁸;
CC Oncogene 11:1469-1474 (1995).
11. FUNCTION: MAY MEDIATES THE PHOSPHORYLATION OF

-1- PTM: PHOSPHORYLATED ON TYROSINE. PHOSPHORYLATION IS PROMINENT DURING EARLY DEVELOPMENT, BUT DECREASES AT LATER EMBRYONIC STAGES

CC AND IN NEWBORN MICE.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS

CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use.

use by non-profit institutions as long as its content is in no way modified and this statement is not removed. Usage by and for commercial entities requires a license agreement (See <http://www.isb-sib.ch/announce/>)

CC	-----	,	-----
DR	EMBL: X90648; CAA62220.1; -		
DR	HSSD: 064010: 1CGR		

```
DR      MGD; MG1:104886; C1K01.
DR      InterPro: IPR000980; -.
DR      InterPro: IPR001452; -.
DR
```

DR Pfam: PF00018; SH3, 1.
DR PRINTS: PR00401; SH2DOMAIN.
DR PRINTS: PR00452; SH3DOMAIN.

KM SH2 domain; SH3 domain; Phosphorylation.

FT	DOMAIN	123	183	SH3.
FT	DOMAIN	235	296	SH3.
SO	SEQUENCE	303 AA:	33817 MW:	R8126DDEPF2053573 CRC64:

Query Match 52.68; Score 911.5; DB 1; Length 303;

Matches	183;	Conservative	34;	Mismatches	57;	Indels	53;	Gaps	6;
5	AGNDFSEFRSSWYGR.LSROEAVALLGGORHGFVLRDSTSPGDYVLVSSENSRVSHY	64							

3 SARFDSSDRSAMYMGPYTRQEAQTRLQGGRRHGMFLVRDSSSTCPGPDYLYLSVSENSRVSHYI 62

```

Db      63  INSLPNR-----RRKIGDDEFDHLLPALLEPYKIHILDTTTLIEPAPRY 105

```

124 -----SKGSSVILIKRKEAEVIRALDEFGNGDEEDLDFPKKGLIKLRDRPEEQWNAED 177
106 PSPPVGSVASAPLPTAEENLEVYRTLYDFPGDAEDLDFPKKGLLVILIEKPEEQMSART 165

QY 178 SSGKRGRIIPVPEVEKIRPASAASVALIGNGDEGSH-----PDPLGGEPFG-PIAQPESVNTP 232
 ::: ||||| |
Db 166 KDRGVGIIPVPVEK-----LVRSPLPGKHGRNSNRYGIEPPAHAAVOPTTP 215
 ::: ||||| |

0Y	233	LPNL-----	QNGSPYARVLOKRVPNAYDKTALALEVGEVLKVTKINS	278
		:	:	

279 EGECNGRGHEPETHVALLDQNPDED 305

DD	2/6	EGEVENGRKGLPEFTHYKLEDDQNPDDN	302
----	-----	------------------------------	-----

GAGC_AVISC		
ID	GAGC_AVISC	
AC	P05433: 085486:	STANDARD; PRT; 440 AA.

DT	01-NOV-1988	(rel. 09, Created)
DT	01-NOV-1988	(rel. 09, Last sequence update)
DT	15-JUL-1998	(rel. 36, Last annotation update)

OS Avian sarcoma virus (strain CT10).
OC Viruses; Retroloid viruses; Avian type C retroviruses.
NX NCBI TaxID=11878; Retroviridae;

RN 111
 RP SEQUENCE FROM N.A.
 RX MEDLINE=88156964; PubMed=2450282;

RA Mayer B.J., Hamaguchi M., Hanafusa H.;
 RT "A novel viral oncogene with structural similarity to phospholipase
 C";
 RL Nature 332:272-275(1998).
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 1 SH3 DOMAIN.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL: Y00302; CA68407.1; -;
 DR PIR: A29851; A29851.
 DR PIR: B29851; TVEV10.
 DR PIR: S00872; S00872.
 DR HSSP: Q64010; 1CKP.
 DR InterPro: IPR0001452; -;
 DR InterPro: IPR0001452; -;
 DR Pfam: PF00017; SH2; 1.
 DR Pfam: PF00018; SH3; 1.
 DR PRINTS: PR00401; SH2DOMAIN.
 DR PRINTS: PR00452; SH3DOMAIN.
 DR PROSITE: PS50001; SH2; 1.
 DR PROSITE: PS50002; SH3; 1.
 KM Oncogene; Polyprotein; SH3 domain; SH2 domain.
 FT DOMAIN 1 208 GAG.
 FT DOMAIN 209 437 CRK.
 FT DOMAIN 438 440 GAG.
 FT DOMAIN 248 354 SH2.
 FT DOMAIN 368 428 SH3.
 SQ SEQUENCE 440 AA; 47176 MW; 0DB5438628982AC CRC64;
 Query Match 47.2%; Score 818.5; DB 1; Length 440;
 Best Local Similarity 77.3%; Pred. No. 7.5e-52;
 Matches 157; Conservative 16; Mismatches 29; Indels 1; Gaps 1;
 QY 5 AGNFDSEBSWTWGRSLRQEAVALLOGRHGVLYVDSSTSGDYLSVSENSRVSHYI 64
 DB 237 AGGFDSDDRSQWYGRSLRQDAVSLLOGRHGVLYVDSSTSGDYLSVSENSRVSHYI 296
 QY 65 INSSGPPVPSPAPOP-PPGVSPSRRLRGDOFDSLPLALFFYKTHYIDTTLIEPVAR 123
 DB 297 VNSLGRPGGRAGGEGPAGLNPTRLIGDQVDSLPLSLEYKTHYIDTTLIEPVSR 356
 QY 124 SRQSGVILLRQEAEEVYRALFDENGDEBDLPKKGDIILIRDKPEQWMNNAEDSGKRG 183
 DB 357 SRQNSGVILLRQEEVEYVYRALFDKGNDDGLDPKKGDIILIRDKPEQWMNNAEDMDGKRG 416
 QY 184 MIPVYVEKYPASASVSLIGG 206
 DB 417 MIPVYVEKCPSSASVSTLTGG 439
 RESULT 9
 CRK_DROME STANDARD; PRT; 271 AA.
 ID CRK_DROME
 AC 09XIM0;
 DT 01-OCT-2000 (Rel. 40, Created)
 DT 01-OCT-2000 (Rel. 40, Last sequence update)
 DT 01-OCT-2000 (Rel. 40, Last annotation update)
 DE ADAPTER MOLECULE CRK.
 GN CRK OR CG1587.
 OS Drosophila melanogaster (Fruit fly).
 OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
 OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;
 OC Ephydroidea; Drosophilidae; Drosophila.
 OX NCBI_TaxId=7227;
 RN [1]

RP SEQUENCE FROM N.A. AND CHARACTERIZATION.
 RC TISSUE=Embryo;
 RX MEDLINE=99173888; PubMed=10072777;
 RA Galletta B.J., Niu X.-P., Erickson M.R., Abmayr S.M.;
 RT "Identification of a Drosophila homologue to vertebrate Crk by
 RT interaction with MBC";
 RL Gene 228:243-252(1999).
 RP [2]
 RP SEQUENCE FROM N.A.
 RC STRAIN=BERKELEY;
 RX MEDLINE=20196006; PubMed=10731132;
 RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,
 RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,
 RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,
 RA Sutton G.G., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,
 RA Brandon R.C., Rogers J.-H.C., Blazey R.G., Champe M., Pfeiffer B.D.,
 RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,
 RA Abril J.F., Agbayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,
 RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,
 RA Beeson K.Y., Berno P.V., Bernier B.P., Bhandari D., Bolshakov S.,
 RA Borkova D., Botchan M.R., Bouck J., Brokstein P., Brotler P.,
 RA Burlis K.C., Busam D.A., Butler H., Cadden E., Center A., Chandra I.,
 RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,
 RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,
 RA Dodson K., Dou P.L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,
 RA Durbin K.J., Evangelista C.C., Ferraz C., Ferreira S., Fleischmann W.,
 RA Foster C., Gabrielian A.E., Garg N.S., Gelbart W.M., Glasser K.,
 RA Glodek A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,
 RA Harris N.L., Harvey D., Helman T.J., Hernandez J., Houck J.,
 RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Idegawa C.,
 RA Jaitani M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Ketchum K.A.,
 RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,
 RA Lascko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,
 RA Liu X., Mattei B., McIntosh T.C., McLeod M.P., McPherson D.,
 RA Merkulov G., Milshina N.V., Mobarry C., Morris J., Mosnelli A.,
 RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,
 RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Paclet J.M.,
 RA Palazzolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,
 RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,
 RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,
 RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,
 RA Svirskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,
 RA Wang Z.-Y., Wassarman D.A., Weinstock G.M., Weissbach J.,
 RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,
 RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,
 RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,
 RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;
 RT "The genome sequence of Drosophila melanogaster";
 RL Science 287:2185-2195(2000).
 CC -1- FUNCTION: ADAPTER PROTEIN WHICH INTERACTS WITH C-TERMINAL PORTION
 CC OF MBC, HOMOLOG OF HUMAN DOCK180. MAY PLAY A ROLE IN CELLULAR
 CC PROCESSES THROUGHOUT DEVELOPMENT.
 CC -1- TISSUE SPECIFICITY: EMBRYONIC ZYGOTIC EXPRESSION IS SEEN IN
 CC INVAGINATING PRESUMPTIVE MESODERM AND ECTODERMALLY DERIVED TISSUES
 CC DURING GASTRULATION. AT STAGE 8, EXPRESSION IS ALSO SEEN IN
 CC ANTERIOR AND POSTERIOR MIDGUT AND CEPHALIC FURROW. BY STAGE 9,
 CC EXPRESSION IS HIGHEST IN VISCERAL MESODERM OF ANTERIOR AND
 CC POSTERIOR MIDGUT, VENTRAL NERVE CORD AND SOMATIC MESODERM.
 CC -1- DEVELOPMENTAL STAGE: EXPRESSED BOTH MATERNALLY AND ZYGOTICALLY
 CC THROUGHOUT EMBRYOGENESIS, DECLINES DURING LARVAL STAGES AND
 CC REAPPEARS DURING PUPATION.
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
 CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
 CC -----
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration
 CC between the Swiss Institute of Bioinformatics and the EMBL outstation-
 CC the European Bioinformatics Institute. There are no restrictions on its
 CC use by non-profit institutions as long as its content is in no way
 CC modified and this statement is not removed. Usage by and for commercial
 CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
 CC or send an email to license@isb-sib.ch).
 CC -----
 DR EMBL: AE003844; AAP59362.1; -;

```

DR EMBL: AF112976; AAD28428.1; -.
DR HSSP: Q64010; 1CKA.
DR FlyBase: FBgn0024811; Crk.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 1.
DR PRINTS: PR00401; SH2DOMAIN.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 1.
DR SH2 domain; SH3 domain; Developmental protein.
FT DOMAIN 12 114 SH2.
FT DOMAIN 117 165 SH3.
FT DOMAIN 220 259 SH3.
SQ SEQUENCE 271 AA; 31205 MW; D1BAFEA3150932DC CRC64;

Query Match 37.1%; Score 642.5; DB 1; Length 271;
Best Local Similarity 43.8%; Pred. No. 1.8e-39;
Matches 133; Conservative 42; Mismatches 68; Indels 61; Gaps 6;

QY 8 FDSERSSWYMGRLSROEVALLOGOR-HGEVLVROSTSPGQYVLSVSENSVSHYITN 66
DB 4 FDSVDRNSWTFGPMRSODATEVLMNEREGVFLVRSNSIAGYVLCVREDTFVSNYITN 63
QY 67 SSGFRPPVPSPAPQPPGVPSPRLIGDQEPDSLPALEFYKIHLYDTTLLIPVARSQ 126
DB 64 KYGQGDQIV-----YRIGDQSFNDLPKLLTFTYTHLYDTTLTKRPACR--- 106
QY 127 GSGVILROEAEYRALPDRNGNDEEDLPKKGDIIRDKPEEOMWNAEDSGKRGMP 186
DB 107 -----RVEKYIGKFDVGSDDDLPFQRGVEVLTVKDEQWMTARNSSGKIGQILP 157
QY 187 VPYVEKY-----RPASVSALIGQNEGSHPPLEGPERGPVPAQSVMPPLP 234
DB 158 VPIYQDIDYDMEADAIKNEPSISGSSNVPESTLK-----KIDLNKKL- 200
QY 235 NLONGPIYARVIOKRVNAYDKTALALEVELYKVKINVGOMEGECNGKRGHPFTYH 294
DB 201 -----PAYARVKOSRVPNAYDKTALKLEIGDITKVTKTININGQMEGLNKGHPFTYH 255
QY 295 RLID 298
DB 256 EFVD 259

RESULT 10
GRAP_HUMAN STANDARD; PRT; 217 AA.
ID GRAP_HUMAN
AC Q13588;
DT 15-DEC-1998 (Rel. 37, Created)
DT 15-DEC-1998 (Rel. 37, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE GRB2-RELATED ADAPTOR PROTEIN.
GN GRAP.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homiinae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=96218119; PubMed=8647802;
RA Feng G.-S., Ouyang Y.-B., Hu D.-P., Shi Z.-Q., Genz R., Ni J.;
RT "Grp is a novel SH3-SH2-SH3 adaptor protein that couples tyrosine
RT kinases to the Ras pathway.";
RT J. Biol. Chem. 271:12129-12132(1996).
CC -1- FUNCTION: COUPLES SIGNALS FROM RECEPTOR AND CYTOPLASMIC TYROSINE
CC KINASES TO THE RAS SIGNALING PATHWAY.
CC -1- SUBUNIT: ASSOCIATES THROUGH ITS SH2 DOMAIN WITH LIGAND-ACTIVATED
CC RECEPTORS FOR STEM CELL FACTOR (KIT) AND ERYTHROPOIETIN (EPOR).
CC ALSO FORMS A STABLE COMPLEX WITH THE BCR-ABL ONCOPROTEIN. GRAP IS
CC ASSOCIATED WITH THE RAS GUANINE NUCLEOTIDE EXCHANGE FACTOR SOS1,

```

```

CC CC PRIMARILY THROUGH ITS N-TERMINAL SH3 DOMAIN.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
CC CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL Outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (see http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL: U52518; AAC50541.1; -.
DR MIM: 604330; -.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 2.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 2.
KW SH2 domain; SH3 domain.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT DOMAIN 156 215 SH3.
SQ SEQUENCE 217 AA; 25336 MW; 09FEC2F3BAC0FAF8 CRC64;

Query Match 14.8%; Score 257; DB 1; Length 217;
Best Local Similarity 31.4%; Pred. No. 6.6e-12;
Matches 64; Conservative 40; Mismatches 54; Indels 46; Gaps 9;

QY 2 RGCAG---NFDSESSWYMGRLSROEVALLOGORH-GEVLVROSTSPGQYVLSVSE 56
DB 42 RVEGEFIPKNYIRKVPHPMYSGRISRLAEETLMKRNHLGFLIRESSSGGEFSVSNY 101
QY 57 NSRVSHYII--NSSGPRPPVPSPAPQPPGVPSPRLIGDQEPDSLPALEFYKIHLYDT 114
DB 102 GQVGHFKVLREASG-----KYFLMEKFNLSNLTVDYFR-----T 137
QY 115 TLLIEPVARSROSGVILROE-----AEYRALPDRNGNDEEDLPKKGDIIRDK 167
DB 138 TT---IARKRQ---IFLREDEPLKSPACFAQAFDSADPSQLSFRRGDIIEVLER 190
QY 168 PEEOMWNAEDSEKRGMPVPYVE 191
DB 191 PDPHMKGR-SCGRVGFPPRSTVQ 213

RESULT 11
DRK_DROME STANDARD; PRT; 211 AA.
ID DRK_DROME
AC Q08012; Q9V605;
DT 01-FEB-1995 (Rel. 31, Created)
DT 01-FEB-1995 (Rel. 31, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE PROTEIN E(SeV)2B (SH2-SH3 ADAPTER PROTEIN DRK).
GN DRK OR E(SeV)2B OR CG6033.
OS Drosophila melanogaster (Fruit fly).
OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;
OC Ephydroidea; Drosophilidae; Drosophila.
OX NCBI_TaxID=7227;
RN [1]
RP SEQUENCE FROM N.A.
RX TISSUE=Eye;
RX MEDLINE=93214989; PubMed=8462097;
RA Simon M.A., Dodson G.S., Rubin G.M.;
RT "An SH3-SH2-SH3 protein is required for p21Ras1 activation and binds
RT to sevenless and Sos proteins in vitro.";
RT Cell 73:169-177(1993).
RN [2]

```

RP SEQUENCE FROM N.A.
RC TISSUE-Embryo:
RA MEDLINE-93214990; PubMed-8462098;
RA Olivier J.P., Raabe T., Henkemeyer M., Dickson B., Mbamalu G.,
RA Margolis B., Schlessinger J., Hafen E., Pawson T.,
RT "A Drosophila SH2-SH3 adaptor protein implicated in coupling the
RT sevenless tyrosine kinase to an activator of Ras granule nucleotide
RT exchange, Sos".
RL Cell 73:179-191(1993).
RN [3]
RP SEQUENCE FROM N.A.
RC STRAIN-BERKELEY;
RC MEDLINE-20196006; PubMed-10731132;
RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,
RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,
RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,
RA Sutton G.G., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,
RA Brandon R.C., Rogers Y.-H.C., Blazer R.G., Champe M., Pfeiffer B.D.,
RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,
RA Abril J.F., Adbayanti A., An H.-J., Andrews-Pfankuch C., Baldwin D.,
RA Balles R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,
RA Beeson K.T., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,
RA Borokova D., Botchan M.R., Bouck J., Brokstein P., Brothier P.,
RA Burtis K.C., Busam D.A., Butler H., Cadieu E., Center A., Chandra I.,
RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,
RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,
RA Dodson K., Doup I.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,
RA Durbin K.J., Evangelista C.C., Ferraz C., Ferlita S., Fleischmann W.,
RA Fodor C., Gabrielian A.E., Gary N.S., Gelbart W.M., Glasser K.,
RA Glodok A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,
RA Harits N.L., Harvey D., Heiman T.J., Hernandez J.R., Houck J.,
RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Ibegwam C.,
RA Jalali M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Keithum K.A.,
RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,
RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,
RA Liu X., Matel B., McIntosh T.C., McLeod M.P., McPherson D.,
RA Merkulov G., Milshina N.V., Mobarry C., Morris J., Moshrefi A.,
RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,
RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Pacle J.M.,
RA Palazolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,
RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,
RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,
RA Splitter E., Spradling A.C., Stapleton M., Strong R., Sun E.,
RA Svitskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,
RA Wang Z.-Y., Massarman D.A., Weinstein G.M., Weissbach J.,
RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,
RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,
RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,
RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.,
RT "The genome sequence of Drosophila melanogaster".
RL Science 287:2185-2195(2000).
CC -1- FUNCTION: REQUIRED FOR PROPER SIGNALING BY SEVENLESS. MAY ACT TO
CC STIMULATE THE ABILITY OF SOS TO CATALYZE RAS ACTIVATION BY
CC LINKING SEVENLESS AND SOS IN A SIGNALING COMPLEX. CAN BIND, IN
CC VITRO, TO SEVENLESS AND TO SOS.
CC -1- TISSUE SPECIFICITY: FOUND MAINLY IN THE DEVELOPING EYE AND IN THE
CC ANTENNAL DISK. ALSO OBSERVED IN OTHER IMAGINAL DISKS TESTED AND IN
CC THE EMBRYO.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>
CC or send an email to license@sib-sib.ch).
DR EMBL: L12446; AAA28898.1; -
DR EMBL: L13173; -; NOT ANNOTATED_CDS.
DR EMBL: AE003818; AAF56368.1; -;

DR PIR: A46443; A46443.
DR PIR: A46444; A46444.
DR HSSP: P29354; IGRI.
DR Flybase: FBgn0004638; drk.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 2.
DR PRINTS: PRO0452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 2.
DR SH2 domain; SH3 domain; Transducer.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 151 SH2.
FT DOMAIN 152 211 SH3.
FT MUTAGEN 67 67
FT MUTAGEN R->H: IN SU(SEV11)R1 MUTANT, OMATIDIAL
FT CELL DEVELOPMENT OBSTRUCTION.
FT H->Y: IN E(SEV)2B MUTANT, OMATIDIAL CELL
FT DEVELOPMENT OBSTRUCTION.
SQ SEQUENCE 211 AA; 24435 MW; A1D0614AF358F3C0 CRC64;
Query Match 13.6%; Score 236; DB 1; Length 211;
Best Local Similarity 29.6%; Pred. No. 2.1e-10;
Matches 56; Conservative 37; Mismatches 64; Indels 32; Gaps 5;
OY 7 NFDSESSWVGGRISRGVEAVALLGGRHGVEIVRDSSTSPGVLSVSENSRVSHYITIN 66
DB 51 NIENKNDHWYIGRTIRDAEKLSNKEGAFILRISSSGDLSVCKCDGVQHRKVL 110
OY 67 SSGPRPVPSPAPDPGSPSRILRIGQEPDLSPLALLEFYKIHLYDTTLIEPVARSRQ 126
DB 111 RD-----AQSKEFLVWVKFNSINELVEYHR-----TASVRSQD 144
OY 127 GSGVLRQ--EAEVYRALFPENGDEEDLPFKKGDLIRIDKREQWMADESGRGM 184
DB 145 --VLRIMPEEMLVQALYDFVQESGELDFRRGDVITVDRSDENWNGEIG-NRKG 200
OY 185 IPVPYVERK 193
DB 201 PPAIVTVTPY 209
RESULT 12
GBR2_HUMAN STANDARD: PRT: 217 AA.
AC P29354; 063057; 014450;
DT 01-DEC-1992 (Rel. 24, Created)
DT 01-DEC-1992 (Rel. 24, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GBR2) (ASH PROTEIN).
GN GBR2 OR ASH.
OS Homo sapiens (Human), and Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominoidea; Homo.
OX NCBI_TaxID=9606, 10116;
RN [1]
RP SEQUENCE FROM N.A.
RC SPECIES-Human; TISSUE-Brain;
RC MEDLINE-92354060; PubMed-1322798;
RA Lowenstein E.J., Daly R.J., Batzer A.G., Li W., Margolis B.,
RA Lammers R., Ullrich A., Skolnik E.Y., Bar-Sagi D., Schlessinger J.,
RT "The SH2 and SH3 domain-containing protein GRB2 links receptor
RT tyrosine kinases to ras signaling".
RL Cell 70:431-442(1992).
RN [2]
RP SEQUENCE FROM N.A.
RC SPECIES-Human; and Rat; TISSUE-Brain, and Lung;
RC MEDLINE-93028395; PubMed-1384039;
RA Matuoka K., Yamakawa A., Shibata M., Takenawa T.,
RT "Cloning of ASH, a ubiquitous protein composed of one Src homology
RT region (SH) 2 and two SH3 domains, from human and rat cDNA

RT libraries.".

RT Proc. Natl. Acad. Sci. U.S.A. 89:9015-9019(1992).

RN [3]

RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.

RC SPECIES-Rat; SPRAIN-MSTAR; TISSUE-Brain;

RX MEDLINE-95293967; PubMed-7775438;

RA Matanabe K., Fukuchi T., Hosoya H., Shirasawa T., Matsuoka K.,

RA Miki H., Takenawa T.;

RT "Splicing isoforms of rat Ash/Grb2. Isolation and characterization of

RT the cDNA and genomic DNA clones and implications for the

RT physiological roles of the isoforms.";

RL J. Biol. Chem. 270:13733-13739(1995).

RN [4]

RP SEQUENCE FROM N.A. (ISOFORM GRB3-3).

RC SPECIES-Human; TISSUE-Placenta;

RX MEDLINE-94233382; PubMed-8178156;

RA Fath I., Schweighoffer F., Rey I., Multon M.C., Boiziau J.,

RA Duchesne M., Tocque B.;

RT "Cloning of a Grb2 isoform with apoptotic properties.";

RL Science 264:971-974(1994).

RN [5]

RP SEQUENCE FROM N.A.

RC SPECIES-Human; TISSUE-Epidermis;

RX MEDLINE-99162407; PubMed-10051406;

RA Boemann H., Gehrtisch S., Jaross W.;

RT "The gene structure of the human growth factor bound protein GRB2.";

RL Genomics 56:203-207(1999).

RN [6]

RP ASSOCIATION WITH IRS-1.

RX MEDLINE-93265658; PubMed-8388384;

RA Tobe K., Matuoka K., Tamemoto H., Ueki K., Kaburagi Y., Asai S.,

RA Noguchi T., Matsuda M., Tanaka S., Hattori S., Fukui Y., Akanuma Y.,

RA Yazaki Y., Takenawa T., Kadowaki T.;

RT "Insulin stimulates association of insulin receptor substrate-1 with

RT the protein abundant Src homology/growth factor receptor-bound

RT protein 2.";

RL J. Biol. Chem. 268:11167-11171(1993).

RN [7]

RP ASSOCIATION WITH IRS-1 AND SHC.

RX MEDLINE-93259135; PubMed-8491186;

RA Skolnik E.Y., Lee C.-H., Batzer A., Vicentini L.M., Zhou M., Daly R.,

RA Myers M.J., Jr., Backer J.M., Ullrich A., White M.F., Schlessinger J.;

RT "The SH2/SH3 domain-containing protein GRB2 interacts with tyrosine-

RT phosphorylated IRS1 and Shc: implications for insulin control of ras

RT signaling.";

RL EMBO J. 12:1929-1936(1993).

RN [8]

RP STRUCTURE BY NMR OF 1-56.

RX MEDLINE-97280795; PubMed-9135122;

RA Wittek M., Mappelli C., Lee V., Goldfarb V., Friedrichs M.S.,

RA Meyers C.A., Mueller L.;

RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with

RT a ten-residue peptide derived from SOS: direct refinement against

RT NOESY couplings and 1H and 13C chemical shifts.";

RL J. Mol. Biol. 267:933-952(1997).

RN [9]

RP STRUCTURE BY NMR OF 60-158.

RX MEDLINE-96387228; PubMed-8794768;

RA Thornton K.H., Mueller W.T., McConnell P., Zhu G., Saltiel A.R.,

RA Thanabal V.;

RT "Nuclear magnetic resonance solution structure of the growth factor

RT receptor-bound protein 2 Src homology 2 domain.";

RL Biochemistry 35:11852-11864(1996).

RN [10]

RP STRUCTURE BY NMR OF 53-163.

RX Senior M.M., Frederick A.F., Black S., Perkins L.M., Wilson O.,

RA Snow M.E., Wang Y.-S.;

RT Submitted (JUN-1997) to the PDB data bank.

RN [11]

RP STRUCTURE BY NMR OF 159-215.

RX MEDLINE-95187706; PubMed-7881903;

RA Kohda D., Terasawa H., Ichikawa S., Ogura K., Hatanaka H.,

RA Mandiyan V., Ullrich A., Schlessinger J., Inagaki F.;

RT "Solution structure and ligand-binding site of the carboxy-terminal

RT SH3 domain of GRB2.";

RL Structure 2:1029-1040(1994).

RN [12]

RP X-RAY CRYSTALLOGRAPHY (3.1 ANGSTROMS).

RX MEDLINE-95232505; PubMed-7716522;

RA Maignan S., Guilloteau J.P., Fromage N., Arnoux B., Bequart J.,

RA Ducoux A.;

RT "Crystal structure of the mammalian Grb2 adaptor.";

RL Science 268:291-295(1995).

RN [13]

RP X-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS) OF 56-153.

RX MEDLINE-98308003; PubMed-9642078;

RA Rahnel J., Garcia-Echeveria C., Furet P., Strauss A., Caravatti G.,

RA Fretz H., Schoepfer J., Gay B.;

RT "Structural basis for the high affinity of amino-aromatic SH2

RT phosphopeptide ligands.";

RL J. Mol. Biol. 279:1013-1022(1998).

RN [14]

RP X-RAY CRYSTALLOGRAPHY (2.1 ANGSTROMS) OF 49-163.

RX MEDLINE-99192587; PubMed-10090780;

RA Etimayer P., France D., Gounarides J., Jarosinski M., Martin M.-S.,

RA Rondeau J.-M., Sabio M., Topiol S., Weidmann B., Zurini M., Bahr K.W.;

RT "Structural and conformational requirements for high-affinity binding

RT to the SH2 domain of Grb2(1).";

RL J. Med. Chem. 42:971-980(1999).

CC -!- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF

CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO

CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH

CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH

CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS

CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND

CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.

CC -!- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM

CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR

CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS

CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A

CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.

CC -!- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL

CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED

CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A

CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING

CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH.

CC -!- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY

CC ALTERNATIVE SPLICING.

CC -!- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.

CC -!- SIMILARITY: CONTAINS 1 SH2 DOMAIN.

CC -!- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC -!- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.

CC -----

CC This SWISS-PROT entry is copyright. It is produced through a collaboration

CC between the Swiss Institute of Bioinformatics and the EMBL outstation -

CC the European Bioinformatics Institute. There are no restrictions on its

CC use by non-profit institutions as long as its content is in no way

CC modified and this statement is not removed. Usage by and for commercial

CC entities requires a license agreement (See <http://www.isb-sib.ch/announce/>

CC or send an email to license@sib-sib.ch).

CC -----

DR EMBL: M96995; AAA58448.1; -

DR EMBL: X62852; CAA44664.1; -

DR EMBL: X62853; CAA44665.1; -

DR EMBL: D49846; BAA08645.1; -

DR EMBL: L29511; AAC37549.1; -

DR EMBL: AF063618; AAC72075.1; -

DR EMBL: AF063614; AAC72075.1; JOINED.

DR EMBL: AF063615; AAC72075.1; JOINED.

DR EMBL: AF063616; AAC72075.1; JOINED.

DR EMBL: AF063617; AAC72075.1; JOINED.

DR PIR: A43321; A43321.

DR PIR: A43321; A43321.

DR PIR: S26050; S26050.

DR PDB: 1GRI; 08-MAR-96.

DR PDB: 1GFC; 31-AUG-94.

DR PDB: 1GFD; 31-AUG-94.

```

DR PDB; 1GHU; 27-JAN-97.
DR PDB; 1TZE; 07-JUL-97.
DR PDB; 1FHS; 17-JUN-98.
DR PDB; 1BM2; 05-AUG-98.
DR PDB; 1BM3; 29-JUL-98.
DR PDB; 1ZFP; 30-MAR-99.
DR MIM; 108355; -.
DR InterPro; IPR000980; -.
DR InterPro; IPR001452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 2.
DR PRINTS; PR00401; SH2DOMAIN.
DR PRINTS; PR00452; SH3DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 2.
KW SH2 domain; SH3 domain; Alternative splicing; 3D-structure.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT VARSPLIC 156 215 SH3.
FT VARSPLIC 60 100 MISSING (IN ISOFORM GRB3-3).
FT VARSPLIC 157 170 MISSING (IN ISOFORM ASH-M).
FT MUTAGEN 49 49 P->L: INEFFECTIVE IN DNA SYNTHESIS.
FT MUTAGEN 203 203 G->R: INEFFECTIVE IN DNA SYNTHESIS.
SQ SEQUENCE 217 AA; 25206 MW; 83A4B0BA1B248DC4 CRC64;

Query Match 12.9%; Score 224; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 1.6e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSESSWYWGRLSROEAVALLQGRH-GVFLVRSSTSPGQDYLVSVSENSRVSHYII 65
DB 51 NYEMKPHMPEFGFKIDIRAKAEEMLSKQRDGAFLINESAPGDFSLVSKFGNDVQHFV 110
QY 66 NSGSPRPVPPSAQPPGVSPSLRIGQEDPSLPALLEFKIKHLDITTLIEPYARR 125
DB 111 LRDG-----AKRYLWYVKFNSINELVDYHR-----STS-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLAFDNGNDEDLPPKKGDIIRIRKPPEOMNANEDSG 180
DB 145 Q---ILRIQIEVQPGQPTVYQALFDPDQDEGLGRDRDFTIHVMDNSDPNMWKKGA-CHG 200
QY 181 KRGMIPVYV 190
DB 201 QTGMPPRNVY 210

RESULT 13
GRB2_MOUSE STANDARD; PRT; 217 AA.
ID GRB2_MOUSE O61240;
AC 060631; O61240;
DT 01-NOV-1997 (Rel. 35, Created)
DT 01-NOV-1997 (Rel. 35, Last sequence update)
DT 15-JUL-1999 (Rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GRB2).
GN GRB2.
OS Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC STRAIN=BAIB/C.
RX MEDLINE=93360985; PubMed=7689150;
RA Suen K., Bustelo X.R., Pawson T., Barbacid M.;
RT "Molecular cloning of the mouse grb2 gene: differential interaction
RT of the Grb2 adaptor protein with epidermal growth factor and nerve
RT growth factor receptors."
RL Mol. Cell. Biol. 13:5500-5512(1993).
RN [2]
RP SEQUENCE FROM N.A. (ISOFORM GRB3-3).
RC STRAIN=BAIB/C;

```

```

RA Tanaka S.;
RL Submitted (JUN-1996) to the EMBL/GenBank/DBJ databases.
RN [3]
RP STRUCTURE BY NMR OF 1-59.
RX MEDLINE=97280795; PubMed=9135122;
RA Wittekind M., Meppell C., Lee V., Goldfarb V., Friedrichs M.S.,
RA Meyers C.A., Mueller L.;
RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with
RT a ten-residue peptide derived from SOS: direct refinement against
RT NOES, J-couplings and 1H and 13C chemical shifts."
RL J. Mol. Biol. 267:933-952(1997).
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK. PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
CC -1- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL
CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED
CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A
CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING
CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH
CC (BY SIMILARITY).
CC -1- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY
CC ALTERNATIVE SPLICING.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC CC
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL; U07617; AAB40022.1; -.
DR EMBL; D85748; BAA12862.1; -.
DR PDB; 1GBQ; 04-SEP-97.
DR PDB; 2GBQ; 04-SEP-97.
DR PDB; 3GBQ; 04-SEP-97.
DR PDB; 4GBQ; 04-SEP-97.
DR PDB; 1GBR; 26-JAN-95.
DR MGD; MGI:95805; Grb2.
DR InterPro; IPR000980; -.
DR InterPro; IPR001452; -.
DR Pfam; PF00017; SH2; 1.
DR Pfam; PF00018; SH3; 2.
DR PRINTS; PR00401; SH2DOMAIN.
DR PRINTS; PR00452; SH3DOMAIN.
DR PROSITE; PS50001; SH2; 1.
DR PROSITE; PS50002; SH3; 2.
KW SH2 domain; SH3 domain; Alternative splicing; 3D-structure.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT VARSPLIC 156 215 SH3.
FT VARSPLIC 60 100 MISSING (IN ISOFORM GRB3-3).
SQ SEQUENCE 217 AA; 25238 MW; 97FA4FE4B248DDE CRC64;

Query Match 12.9%; Score 224; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 1.6e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSESSWYWGRLSROEAVALLQGRH-GVFLVRSSTSPGQDYLVSVSENSRVSHYII 65
DB 51 NYEMKPHMPEFGFKIDIRAKAEEMLSKQRDGAFLINESAPGDFSLVSKFGNDVQHFV 110
QY 66 NSGSPRPVPPSAQPPGVSPSLRIGQEDPSLPALLEFKIKHLDITTLIEPYARR 125
DB 111 LRDG-----AKRYLWYVKFNSINELVDYHR-----STS-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLAFDNGNDEDLPPKKGDIIRIRKPPEOMNANEDSG 180
DB 145 Q---ILRIQIEVQPGQPTVYQALFDPDQDEGLGRDRDFTIHVMDNSDPNMWKKGA-CHG 200
QY 181 KRGMIPVYV 190
DB 201 QTGMPPRNVY 210

```

```

Db 51 NYTEMKPHWFECKIPRAKAEEMLSKQRHDAFLIRESEAPGDSLSVKGNVQHFV 110
QY 66 NSSGPRPVPPSPAPCPGVSPSRLRIGDQEPDSLALLEFYKHYLDTTLLIEPVARS 125
Db 111 LRDG-----AGKYFLWVVKNSINELVDYHR-----STS-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLFPDNGNDEEDLPFKKGDIIRIDKPEEQMNAEDSEG 180
Db 145 Q---IFLRIDIEQYPOQPTVQALFDPDPEDEGLGFRKGDFTLVNDSDPMWKA-CHG 200
QY 181 KRGMIPIPVY 190
Db 201 QTGMFPRNV 210

RESULT 14
GRB2_CHICK STANDARD; PRT; 217 AA.
ID GRB2_CHICK AC 007883;
DT 01-FEB-1995 (rel. 31, Last sequence update)
DT 01-FEB-1995 (rel. 31, Last sequence update)
DT 15-JUL-1999 (rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
GN (SH2/SH3 ADAPTER GRB2) (ASH PROTEIN).
OS Gallus gallus (Chicken).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC Gallus.
OX NCBI_TaxID=9031;
RN 11)
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RX MEDLINE=94085795; PubMed=8262390;
RA Masenius V.-M., Merilainen J., Lehto V.-P.;
RT "Sequence of a chicken cdna encoding a GRB2 protein."
RL Gene 134:299-300(1995).
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
CC -1- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@sib-sib.ch).
CC -----
DR EMBL: LI9258; AAA16318.1; -.
DR PIR: J70664; J70664.
DR HSSP: P29354; 1GRI.
DR InterPro: IPR0000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 2.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS00001; SH2; 1.
DR PROSITE: PS00002; SH3; 2.
KM SH2 domain; SH3 domain.

```

```

FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT DOMAIN 156 215 SH3.
SQ SEQUENCE 217 AA; 25076 MW; DDC9A84ECDG52859 CRC64;

Query Match 12.6%; Score 218; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 4.2e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NPDSEKRSWYMGRLSGROAVALLQGOHRH-GVELYRDSSTSPGVYLSVNSRSXYII 65
Db 51 NYTEMKPHWFECKIPRAKAEEMLSKQRHDAFLIRESEAPGDSLSVKGNVQHFV 110
QY 66 NSSGPRPVPPSPAPCPGVSPSRLRIGDQEPDSLALLEFYKHYLDTTLLIEPVARS 125
Db 111 LRDG-----AGKYFLWVVKNSINELVDYHR-----STS-----VSRNQ 144
QY 126 QGSGVILRQ-----EEAEYVRLFPDNGNDEEDLPFKKGDIIRIDKPEEQMNAEDSEG 180
Db 145 Q---IFLRIDIEQYPOQPTVQALFDPDPEDEGLGFRKGDFTLVNDSDPMWKA-CHG 200
QY 181 KRGMIPIPVY 190
Db 201 QTGMFPRNV 210

RESULT 15
GRB2_XENLA STANDARD; PRT; 217 AA.
ID GRB2_XENLA AC P87379;
DT 15-DEC-1998 (rel. 37, Created)
DT 15-DEC-1998 (rel. 37, Last sequence update)
DT 15-JUL-1999 (rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
GN (SH2/SH3 ADAPTER GRB2).
OS Xenopus laevis (African clawed frog).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidoidea; Pipidae;
OC Xenopodidae; Xenopus.
OX NCBI_TaxID=6355;
RN 11)
RP SEQUENCE FROM N.A.
RA Lu W., Mayer B.-J.;
RL Submitted (Feb-1997) to the EMBL/Genbank/DBJ databases.
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS (BY
CC PROTEINS IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS (BY
CC SIMILARITY).
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE (BY SIMILARITY).
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@sib-sib.ch).
CC -----
DR EMBL: U89775; AAB49699.1; -.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.

```

